Direct reprogramming of fibroblasts into functional cardiomyocytes by defined factors.

Public Summary:

We show in this paper that the cells of the heart that normally form scar tissue after a heart attack can be turned directly into beating heart cells, using a "cocktail" of factors that turn on heart genes.

Scientific Abstract:

The reprogramming of fibroblasts to induced pluripotent stem cells (iPSCs) raises the possibility that a somatic cell could be reprogrammed to an alternative differentiated fate without first becoming a stem/progenitor cell. A large pool of fibroblasts exists in the postnatal heart, yet no single "master regulator" of direct cardiac reprogramming has been identified. Here, we report that a combination of three developmental transcription factors (i.e., Gata4, Mef2c, and Tbx5) rapidly and efficiently reprogrammed postnatal cardiac or dermal fibroblasts directly into differentiated cardiomyocyte-like cells. Induced cardiomyocytes expressed cardiac-specific markers, had a global gene expression profile similar to cardiomyocytes, and contracted spontaneously. Fibroblasts transplanted into mouse hearts one day after transduction of the three factors also differentiated into cardiomyocyte-like cells. We believe these findings demonstrate that functional cardiomyocytes can be directly reprogrammed from differentiated somatic cells by defined factors. Reprogramming of endogenous or explanted fibroblasts might provide a source of cardiomyocytes for regenerative approaches.

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